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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,427	05/06/2002	Karl Bruce Thor	X-11072	1087

7590 10/03/2006

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EXAMINER	
CHONG, YONG SOO	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 10/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,427	THOR, KARL BRUCE	
	Examiner	Art Unit	
	Yong S. Chong	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-42 and 51-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-42 and 51-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/28/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/28/2006 has been entered.

Claim(s) 1-36, 43-50, 55 have been cancelled. Claim(s) 37-42, 51-54 are pending and examined herein.

Applicant's arguments have been fully considered but found not persuasive. The 103 rejection is maintained for reasons of record and is repeated below for Applicant's convenience.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 37-42 and 51-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over McMahon et al. (*J. Urology*, 161, 1826-30) and Lane (*J.*

Psychopharmacology, 11(1), 72-82) in view of Eli Lily (ZA 9300694) and Robertson et al. (USPN 5135947).

McMahon et al. teaches the treatment of premature ejaculation with oral doses of paroxetine hydrochloride (an SSRI) as needed (Title). The treatment is taught as being administered on an as needed basis without a priming dose 3-4 hours prior to planned intercourse (Abstract). SSRIs are taught in general to delay orgasm and reduce sexual excitement thereby having a beneficial effect on premature ejaculation (2nd and 3rd paragraphs of p. 1826).

Lane teaches SSRIs for the management of premature ejaculation (Abstract; p. 79). Lane also teaches low dosages of SSRIs administered on an as needed basis prior to intercourse for the treatment of premature ejaculation (p. 79, 2nd col., 1st full paragraph).

Eli Lilly teaches the treatment of premature ejaculation with the SSRIs fluoxetine, dapoxetine, and duloxetine (pp. 1 and 5).

Robertson et al. teaches sluoxetine, serotonin and the compounds as instantly claimed as known in the art as SSRIs (col. 1, lines 15-66; col. 3, lines 35-36; col. 23, lines 1-24 and 48-60; col. 24, lines 46-58). Oral administration of the compounds are taught (col. 19, lines 22-24).

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute the specific compounds of McMahon et al. and Lane with the compounds as instantly claimed because (1) McMahon et al. teaches the treatment of premature ejaculation with various SSRIs; (2) McMahon et al. teaches that SSRIs cause

delayed orgasm and reduced sexual excitement thereby having a beneficial effect on premature ejaculation; (3) Lane teaches that SSRIs may be used in the management of premature ejaculation; (4) Eli Lilly teaches the treatment of premature ejaculation with the compounds as instantly claimed; and (5) Roberson et al. teaches the instantly claimed compounds as SSRIs. Accordingly, absent a showing of unexpected results, it would have been obvious to one of ordinary skill in the art to utilize the known SSRIs of Robertson et al. in the treatment of either McMahon et al. or Lane. One would have been motivated to substitute the SSRIs of McMahon et al. and Lane with the SSRIs as instantly claimed because of an expectation of success in treating premature ejaculation with an SSRI, as taught by both McMahon et al. and Lane.

It would have been obvious to one of ordinary skill in the art to administer the instantly claimed compounds in the dosages claimed and at the times claimed because "[w]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Response to Arguments

Applicant argues in the Declaration of David A. Rivas that McMahon et al. conclusions regarding as needed dosing of paroxetine does not allow the skilled artisan to draw any conclusions about whether or not as needed use of paroxetine in the absence of priming doses is efficacious because the "as needed" use of paroxetine in McMahon et al. does not preclude priming doses. Rivas states, "without prior 2 week

daily dosing" in Study 1 is not "in the absence of a priming dose." Rivas also states that the "as needed" use of paroxetine in Study 1 was not designed to avoid a priming dose effect.

The Declaration under 37 CFR 1.132 filed 7/28/2006 is insufficient to overcome the rejection of claims 37-42, 51-54 based upon McMahon et al. as set forth in the last Office action because: the interpretation of the reference by Rivas is incorrect. Nowhere in the reference, especially in Study 1, does it state the need to administer a priming dose or refer to a priming dose effect. In essence, the absence of such statements has prompted the incorrect conclusions concerning the requirement of any priming doses.

Rivas argue that McMahon et al. study design did not impose a minimum time interval between intercourse episodes and therefore, paroxetine from one dose that was not cleared from the body could, in combination with a subsequent dose, result in paroxetine exposure in the patient greater than a single dose, thereby functioning as a priming dose. This is not persuasive because although McMahon et al. states "paroxetine as needed is significantly better if patients are initially treated with the drug daily," there is no doubt that paroxetine still increases mean ejaculatory latency time without daily dosing.

Rivas argue that McMahon et al. does not provide sufficient information to determine whether the week 1 treatment data of Study 1 are statistically significantly different from the control data. Again, an incorrect conclusion is made because although McMahon et al. states statistically superior results for weeks 2-4, this does not

preclude any positive results for week 1. In fact, as reported in Table 2, an increase in ejaculatory latency time was observed in week 1 when compared to the placebo.

Applicant argues, "by [McMahon et al.'s] admission, [] there was no statistically superior increase in ejaculatory latency in the first week." This argument is not persuasive. First, the argument presupposes that the dosing during the first week of administration is, effectively, equivalent to a "priming dose". If such an argument were found to be persuasive, however, it would suggest that for a drug to be administered on an "as needed" basis in the absence of a priming dose, only the first administration of the drug would qualify as "as needed" in the absence of a priming dose. Second, the language of the disclosure clearly suggests that while a priming dose is preferred, it is not required. McMahon states that "paroxetine as needed was significantly better if patients were initially treated with the drug daily." Such a suggestion would indicate to one of ordinary skill in the art that the effects of administration are the best when there is a priming dose, but that the administration of the drug in the absence of a priming dose would also be effective at achieving the desired results. Accordingly, Applicant's suggestion that Examiner is required to provide evidence that the data is of McMahon et al. for the first week is statistically significant when McMahon et al. says that it is not is not necessary. Furthermore, McMahon et al. clearly illustrates (Figure 1) that the mean ejaculatory interval was seen to increase after one week of administration of paroxetine in both Groups A and B by identical amounts and that the increase was more than that observed for placebo. The multiple of increase seen in Groups A and B (weeks 1 and 8, respectively) are comparable to those set forth in the instant specification (see, e.g.,

Table 9). Furthermore, it is noted that McMahon et al. does not state that the results of week 1 are *not* statistically superior. Accordingly, one of skill in the art would look to Fig. 1 to determine the results of week 1, wherein the skilled artisan would observe the increases in mean ejaculatory interval, as discussed above.

Rivas argue against the experimental design with regard to control groups, bias toward a single blind rather than a double blind study, lack of information regarding stopwatch measurement directions, different time periods for measuring pretreatment values of IELT and coitus frequency. This is not persuasive because these factors do not rebut the fact that an increase in increase in ejaculatory latency time was observed in week 1 when compared to the placebo.

Applicant argues that in McMahon et al., "neither the design or the results of the studies would lead one of skill in the art to conclude that an SSRI could be used to treat PE patients on an as-needed basis." This argument is not persuasive because McMahon et al. clearly teaches the administration of the SSRIs therein on an "as needed" basis. See Abstract; p. 1827, Study 1; etc. When the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. *In re Sasse*, 629 F.2d 675, 207 USPQ 107 (CCPA 1980).

Applicant attempt to rebut the presumption of operability of McMahon et al. by arguing that "[t]he McMahon study did not use an appropriate number of men suffering with PE to address the study objective" and that "[t]he McMahon studies were single-

blind studies". These arguments are not persuasive because Applicant's allegation that there are an insufficient number of test subjects does not address the presumption of operability, but the "scientific validity". There is no reasons to assume that the standard required for one of ordinary skill in the art to accept the teachings of McMahon et al. as scientific certainty would be the same as the standard required for one of ordinary skill in the art to *presume* that the invention would *work*. It is further noted that there is no supporting documentation that McMahon's number of test subjects is insufficient for "scientific validity". Applicant's arguments regarding the single-blind studies are, likewise, unpersuasive. Applicant's argument that "on average, trials that have not used appropriate levels of blinding, such as McMahon, show larger treatment effects than blinded studies" is not sufficient to suggest to the skilled artisan that the teachings of McMahon should not be presumed enabled. First, it is noted that the teaching merely suggests that "on average" different levels of blinding produce different results. Second, there is only a suggestion that varying levels of blinding may lead to varying magnitudes of efficacy, not that the efficacy is, itself, questioned.

Applicant argues that because Lane states that "[t]he placebo-controlled studies with sertraline and paroxetine used high doses. The efficacy of the lower doses and different dosing regimens has yet to be fully explored" that Lane "questions the applicability of these two initial reports to the clinical use of sertraline and paroxetine themselves and certainly does not support the general efficacy of SSRIs in the treatment of PE." This argument is not persuasive because Lane does not suggest that the treatment does not work but merely that, as with all drugs, dosage optimization must

be determine and that once such a dosage optimization is determined that a cost/benefit analysis of the side effects and treatment benefits must be weighed.

Applicant argues that Lane's review of Swartz's "seemingly amazing results, that are inconsistent with any results available at that time, or that have been published subsequent to that report appear to have been an average of both daily and as-needed dosing." This argument is not persuasive because even if the results were indeed an average of both daily and as-needed dosing, such an averaging would not take away from the fact that Swartz via Lane clearly teaches administration on an as needed basis.

Applicant argues that the Swartz teaching that "the '26-hour elimination half life [of sertraline] allows considerable liberties in dosing schedules" indicates that the teaching is a "preliminary case report and, even in combination with the high dose studies of paroxetine and sertraline, one of skill in the art clearly would not regard this report as supporting that all SSRIs, administered in low doses on an as-needed basis prior to intercourse would be efficacious in treating PE." This argument is not persuasive because the teaching that there are considerable liberties in dosing schedules indicates merely that there are considerable liberties in dosing schedules or, in other words, that administration schedules may be adjusted to the particular needs of a patient. Furthermore, the Abstract of Lane clearly teaches that "selective serotonin reuptake inhibitors (SSRIs) are clearly associated with delayed ejaculation ...". This teaching, coupled with the other references, particularly Eli Lilly and Robertson et al., that it would have been obvious to treat PE with dapoxetine. Furthermore,

administration of SSRIs on an as-needed basis is disclosed as being efficacious by both Lane and McMahon et al., as discussed above.

Examiner respectfully reminds Applicant that the standard for obviousness is not absolute but a reasonable expectation of success.

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

YSC

S. Wang

SHENGJUN WANG
PRIMARY EXAMINER